

Evaluation of delivery of therapeutics by Dissolving Microneedles

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Abstract

Compared to more traditional routes like oral administration and hypodermic injection, transcutaneous drug delivery through chemical permeation of the skin, iontophoresis, ultrasound, microneedle treatment, or various other strategies has the potential to provide many practical and clinical advantages.¹ Relative to parenteral injection, transcutaneous delivery is non-invasive, potentially allowing for rapid, pain-free administration either by minimally trained health care providers, or through self-administration.^{2, 3} Transcutaneous delivery systems may reduce the generation of dangerous medical waste and inhibit the spread of disease known to occur through needle-reuse and needle-based injury.^{4, 5} Further, dry storage of systems designed for topical application can also provide enhanced drug stability, enabling transport of environmentally sensitive biological therapeutics without the necessity for refrigeration. This is a key issue as the requirement of “cold chain” distribution increases costs and inherently limits the availability of therapies throughout the developing world.² Transcutaneous therapeutic administration also has the potential to enhance the clinical effectiveness of treatment, by allowing for more efficient delivery of drugs susceptible to first-pass metabolism in the liver. Dissolving microneedles are arrays of ultra-small needles made from water-soluble materials typically with lengths in the micrometer range (less than 1000 μm). They create pores in the skin and release drug payload upon microneedle dissolution (dissolving MN).

Dissolving microneedles, mostly using different kinds of Sugars as the matrix, usually release drugs or vaccines quickly in reported that insulin released from microneedles very quickly, and almost all of the formulated insulin was released within 1 hour when dextrin was used as matrix. Nevertheless, sustained release of drugs or vaccines is also required under some circumstances. Prepared microneedles with model drug encapsulated not within the microneedle tips but only in the backing layer, which served as a controlled-release reservoir that delivered molecules by a combination of swelling the backing with interstitial fluid drawn out of the skin and molecule diffusion into the skin via channels formed by dissolved microneedles. They revealed that Sulforhodamine release from carboxymethyl cellulose microneedle patches exhibited an initial lag time of a few hours, followed by steady release for approximately 1 day. Similar behavior was seen for microneedle patches made of amylopectin, but with slower kinetics. In this case, lag time was longer and release took place over a few days. Polymeric dissolving microneedles designed by Donnelly et al have been produced from Gantrez AN-139, and delivered 83% of the encapsulated Kumar et al²⁷ characterized and used maltose microneedles to micro porate full-thickness pig-ear skin

to evaluate drug delivery of model small (calcein) and large (human growth hormone) molecules. It was found that modulated theophylline into porcine skin within 24 hours.²⁶

The modulated ITP protocol resulted in peaks in flux with application of current and gradual decrease with termination of current, and current density and time could be used appropriately to program a desired drug-delivery. Furthermore, it has been shown that the application of an electric current enables the permeation of macromolecules from the entire microneedle-array matrix, and not just that which was contained within the microneedles alone. Thus the application of an electric current significantly increased the extent of macromolecular delivery from the poly(methyl vinyl ether maleic anhydride) microneedle array, which is also promising for the sustained delivery of drugs and vaccines. They concluded that long-acting SDMP preparation would be possible by means of porous silicate adsorbent-held insulin.

The application of nanotechnology in health sciences has experienced an exponential growth over the last 25 years with special focus on drug delivery systems. Transdermal delivery has recently gained importance for its numerous advantages, which include sustainable release, bypass of the pre-systemic hepatic metabolism and patient compliance. Microneedles are designed to circumvent the skin barrier to enhance transdermal drug delivery. They have been produced in various geometries (cone, cylinder, triangular prism, etc) and materials such as silica, polymers or metals. Microneedles made from sugars or water soluble polymers are dissolvable in the skin and release the drug cargo leaving no sharp waste behind. Moreover, polymer microneedles can incorporate larger drug load than other type of needles such as coated or hydrogel swelling microneedles. These dissolving microneedle arrays have been applied in various pharmacological sectors such as gene therapy, vaccine delivery or drug delivery.

However there is still a need of clinical and pre-clinical research before these devices can be released into the market. An essential challenge is to tailor the microneedles dissolution rate to control the release of therapeutics irrespective of the polymeric material. There is also a need to reduce the risk of skin infections during the insertion as microneedles create small pores on the skin.

Our research focuses on the development of plasma polymerized surface engineered microneedles for a controlled dissolution and controlled drug release. This one-step, environmentally friendly and substrate independent technique will also ease the industrial manufacture. Furthermore these surfaces can be functionalize to confer antibacterial properties to our microneedles patches to hinder infections and skin damage.